

The Effect of Aerobic Training on Inflammatory Markers of Cardiovascular Disease Risk in Obese Men

¹M.R. Hamedinia, ¹A.H. Haghighi and ²A.A. Ravasi

¹Department of physical education, Sabzevar Tarbiat Moallem University, Sabzevar, Iran

²Faculty of Physical education, Department of Physical Education and Sport Sciences, University of Tehran, Tehran, Iran

Abstract: The aim of the present research was to study the effect of aerobic training on inflammatory markers of cardiovascular disease risk in obese men. For this purpose, 24 male subjects (age 35-48) (16 obese, 8 lean) involuntarily participated in our study. Obese men were randomly assigned to one of two groups: aerobic training or control group. The 3rd group was called lean men group. Blood samples were taken (5 cc) in fasting state from all subjects. The experimental subjects received aerobic training for 13 weeks, 3 sessions per week. The aerobic training program included continuous running (in gymnasium) with an intensity of 75-85% maximal heart rate. Results showed that aerobic training caused a significant decrease in the serum CRP and WBC levels of the obese men ($P=0.05$). In addition, they determined that in obese men at baseline state serum CRP and WBC concentrations were significantly higher than those in lean men ($P<0.05$). We concluded that aerobic training caused a decrease in the inflammatory markers and probably decreased future cardiovascular risk in obese men.

Key words: Aerobic training % Inflammatory markers % Obesity

INTRODUCTION

Chronic inflammation and thrombosis play a key role in the outbreak and progression of atherosclerosis and in the alteration of an atherosclerosis firm plaque into a transitory and potential impairment [1]. Different studies show the relationship between inflammatory markers and coronary heart disease risk [2, 3].

C-reactive protein (CRP) is the marker of sub-clinical inflammation. An increase in CRP results in a four to fivefold increase in coronary risks [3]. There is a reverse relationship between CRP and sensitivity to insulin and a direct relationship between CRP and type 2 diabetes risk [4]. This protein increases in obese patients [5]. Another inflammatory marker is elevated white blood cells (WBC) count. It is a predictor of mortality resulted from cardiovascular diseases irrespective of smoking and other traditional risks [2, 6]. Even in a natural domain, there is a positive and independent relationship between WBC count and the mortality resulted from coronary heart disease [6]. There is a positive and significant relationship between WBC count and the intensity of atherosclerosis carotid as well [7]. WBC in blood viscosity releases materials which cause the plaques to tear and the

thrombosis to form [8]. WBC plays a role in the endothelial dysfunction as well [9]. Different researches report the relationship between elevated WBC count and the obesity degree [10, 11]. On the other hand, it was shown that physical activity reduced coronary heart disease (CHD) risk [12] although the original mechanism of the reduction is not totally clear.

Recent reports show that inflammatory markers are predictive of an increase in CHD incidence [3, 6].

Therefore, it is rational to suppose that if physical activity decreases CHD risk, the decrease may happen through inflammatory prevention or reduction in some parts. The results of some researches show that there is a relationship between higher levels of physical activity and physical fitness and lower levels of inflammatory markers (WBC, CRP) [13, 14]. On the other hand, few researches have investigated the effect of regular training or aerobic training on the resting levels of inflammatory markers (WBC, CRP) [15, 16]. Anyway, if physical activity proves to decrease inflammation, more researches will be required to determine the mechanism of the decrease and the intensity and duration of the activity causing most decrease of inflammation.

MATERIALS AND METHODS

The research was semi-experimental. 24 subjects (16 obese and 8 lean) were voluntarily selected from Sabzevar Tarbiat Mo'alleh University. They handed on letters of satisfaction to show their interest in participating in this research. One of the compulsory qualifications of the research was the lack of physical activity record, illness and smoking in the subjects. They were divided into obese and lean groups based on their body fat percentage; the obese group consisted on the men with body fat percentage of 20 or more and the lean group with body fat percentage of 10 or less. The age, height, weight, body fat percentage and maximal aerobic capacity of all subjects were measured in sport physiology laboratory. To make the groups homogeneous, the information from sport physiology laboratory was added to the information about medical record and the readiness to start physical activity (obtained from self-evaluation of health status questionnaires). Then, the obese men were divided randomly into two groups of endurance training (8 members) and control (8 members).

Blood Samples and Biochemical Markers: To examine the biochemical variables, blood samples were gathered after 12 to 14 hours of fasting. First, the subjects were required not to perform any physical activity two days before the test. 5 cc of blood was obtained from each subject's left-hand vein in sitting and resting statuses. 2 cc was used to determine WBC. The serum from the remaining 3 cc was kept at -80°C so that it could be used later to measure CRP. Then, the subjects performed 13 weeks of endurance training. 48 hours after the last training session, the blood samples were obtained from the experimental and control groups like the first stage. Cell counter set was used to measure WBC and an especial kit with Elisa method to measure CRP.

Endurance Training: Endurance training consisted of 13 weeks and 3 sessions per week. Each session included 20-minute warm-up via different running, stretching, limbering up and jumping activities. Then, a continuous running with a stable trend and an intensity of 75-85% maximal heart rate was performed. The running took 15 minutes in the first session. One minute was added to the running time each two sessions so that the running time increased to 30 minutes. This period was retained till the

last training session (the end of 13th week). Maximal heart rate was measured by the 220-age formula and the intensity of training measured by heart rate monitoring belt. At the end of each session, cool-down was performed via light running, stretching and limbering up activities for 10 minutes.

VO2Max: To measure this marker, YMCA (Young Man Christian Association) sub-maximal cycle ergometer test was used.

Body Fat Percentage: Subjects' hypodermic fat was measured using caliper in three parts of chest, stomach and thigh by Jackson and Pollack [17].

Statistical Tests: Descriptive statistics was used to calculate the central markers and the dispersion and one-way variance analysis test to investigate the homogeneity of the groups and also to compare each variable in the three groups before the application of the independent variable. As they were meaningful, Bonferroni post hoc test was used. Independent t test was used to compare the averages of aerobic and control posttests. All the statistics was performed using SPSS software and $P < 0.05$ was considered [18].

RESULTS AND DISCUSSION

The result of one-way variance analysis of all variables (except for VO2max) presented in Table 1 showed that there was a meaningful difference among the three groups. Bonferroni post hoc test showed that the difference existed between the lean group and the two obese groups ($P < 0.05$). The age, height and received calorie were compared between the experimental and control groups and the result showed that they were equal in the baseline. The variables were as follows in the experimental group: 41.33 ± 5.1 years old, 172.77 ± 6.02 cm and 2870 ± 270 calorie and as follows in the control group: 38.62 ± 3.15 , 172 ± 5.4 and 3000 ± 225 .

The results of independent t test in weight ($P = 0.592$) and body mass ($P = 0.562$) markers showed that there was no meaningful difference between the two groups. Therefore, it can be said that the aerobic training did not meaningfully affect the mentioned variables (Table 2).

The results of independent t test in other variables in Table 2 showed that there was a meaningful difference between the two groups. It can be said that the endurance training resulted in their meaningful decrease.

Table 1: Physical, physiology and biochemical markers in experimental and control groups before training

Marker	Group			P
	Endurance training	Control	Lean	
Weight (kg)	83.05±6.76	83.62±10.99	57.75±4.83	0.001
Body fat percentage (%)	22.83±1.88	25.61±4.16	8.32±2.07	0.001
Body mass marker (kg/m ²)	27.92±2.17	29.42±4.59	17.13±6.71	0.001
VO2max (ml/kg/min)	26.33±4.82	23.00±6.36	29.00±4.34	0.284
CRP	1.15±0.57	1.13±0.60	0.26±0.21	0.002
WBC	8.57±1.19	8.67±1.16	5.87±0.85	0.001

The scores are presented in an average and SD frame

Table 2: Physical, physiological and biochemical markers of experimental and control groups after physical activity

Marker	Group		P
	Endurance training	Control	
Weight (kg)	83.83±7.34	84.43±8.99	0.592
Body fat percentage (%)	19.53±3.02	26.47±3.60	0.001
Body mass marker (kg/m ²)	27.81±2.14	29.42±4.59	0.562
VO2max (ml/kg/min)	33.22±4.82	20.50±5.04	0.001
CRP	0.56±0.43	1.05±0.51	0.048
WBC	6.81±0.82	8.35±0.63	0.004

The scores are presented in an average and SD frame

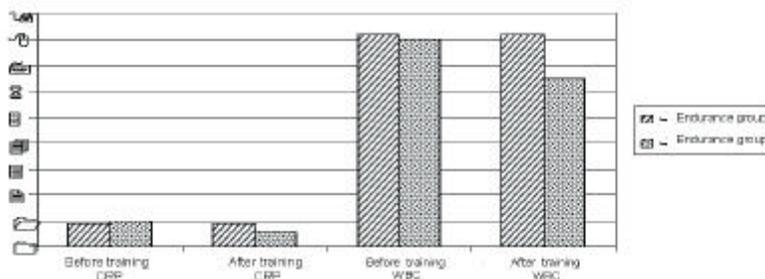


Fig. 1: Dependent variables before and after the training

DISCUSSION

The main finding in this research was that the aerobic training meaningfully decreases WBC and CRP in obese men. Past researches show a meaningful and reverse relationship between regular physical activity and the mentioned markers [13, 14]. These researches report that those who are physically more active and fit, have lower levels of inflammatory markers. The results of some other studies show that long-term aerobic training decreases serum CRP [15, 16]. However, as far as we know, there are no researches on the effect of regular training on WBC. The results of this research showed that the effect of aerobic training on CRP (49.38% decrease) and on WBC

(20.34% decrease) was not equal. This difference can be due to different reactions of inflammatory markers to inflammatory cytokines as a part of the severe level reaction. Probably, physical activity presents its cardio-protector effects by a number of mechanisms. These mechanisms include direct effects on cardiovascular system with elevated stroke volume [11] and elevated O₂ max consumption [19]. Training as well increases the dimensions of coronary artery in animal models [20]. Apparently, long-term endurance training directs the coagulation system toward a fibrinolytic activity preferably toward a thrombosis activity through an increase in the activity of the plasminogen activator of the tissue and a decrease in the activity of the plasminogen

activator inhibitor [21]. This agreement is contrary to the role of elevated leukocyte count in the outbreak of cardiovascular disease via microvasculature blockage and elevated hypercoagulability and fast spread of heart stroke [2]. The relationship between physical activity and lower levels of inflammation can suggest another heart-protector mechanism. The prevalent concept about inflammatory patho-physiological mechanisms connected to atherosclerosis is inflammatory cytokines produced as a result of oxidized LDL stimulator and macrophages accompanying atherosclerosis plaques [22]. Inflammatory cytokines produced during this process are IL-1B, IL-6 and TNF- α . Laboratory studies show that different combinations of these cytokines stimulate the production of CRP [23] and leukocytosis [24]. Researches showed that regular physical training decreases oxidized LDL [24] and also serum levels of TNF- α and IL-6 [15, 16]. Therefore, the effect of regular training on the TNF- α and IL-6 levels can be responsible for WBC and CRP decrease in the experimental group. Also, the relationship between physical activity and lower levels of inflammation can be created through the relationship between endurance training and lower levels of general and stomach obesity. It is shown that the obese people compared with lean people produce higher levels of inflammatory mediators such as IL-8, TNF- α and IL-6 [25]. Endurance training can decrease the production of the inflammatory mediators from lipid tissues and increase the production of the anti-inflammatory mediators such as IL-10 from lipid tissues through the direct effect on fat tissues and elevated lipolysis and through an increase in lipase activity sensitive to hormone [26]. The consequences of these changes show that the aerobic training can decrease the inflammatory markers of blood circulation (WBC, CRP) through a decrease in inflammation resources.

It is known that insulin resistance accompanies inflammation [27]. Past researches showed the relationship between WBC and CRP and insulin resistance [27, 28]. Also, it is shown that physical activity can decrease insulin resistance [29]. This proposes that probably the convalescence of insulin sensitivity by physical activity results in lower levels of inflammation and WBC and CRP decrease.

Aerobic training can increase the plasma volume. This agreement recovers blood viscosity and decreases leukocytosis count in each unit of blood volume. Consequently, obesity results in oxidative stress [30]. On the contrary, there are evidences from human and animal researches showing that long-term aerobic training can decrease the oxidative stress to a great extent though the

elevated capacity of antioxidant defense [31]. This agreement decreases the inflammation.

This research showed that there was a meaningful difference in serum CRP and WBC between lean and obese groups. Past researches reported a positive and meaningful relationship between WBC and CRP and obesity [5, 10, 11]. The result of this research is in accordance with the findings of the above-mentioned researches. The mechanism of the elevated inflammatory markers in obese men compared to lean group can be interpreted that obesity results in a slight chronic inflammation. Lipid tissue is considered as an endocrine organ due to different secretions such as TNF- α and IL-6 [32]. It is shown that TNF- α stimulates the production of IL-6 and IL-6 greatly stimulates the production of hepatic CRP as well [33]. Therefore, the elevated lipid tissue in obese people results in the elevated serum CRP (cascade). It is also shown that WBC production is stimulated by cytokines secreted from lipid tissues especially IL-6 and IL-8 [34]. Therefore, higher amount of these cytokines in obese men compared to lean group [25] causes an increase in WBC in the obesity status. On the other hand, it is clear that obesity causes insulin resistance [35]. Past researches show a positive and meaningful correlation between WBC and CRP and insulin resistance [27, 28]. It is shown that there is a relationship between IL-6 level of blood circulation and fasting insulin and blood pressure [36] and as insulin decreases the mediation of the severe level reaction by IL-6 [37], insulin resistance can result in more concentrations of inflammatory markers (CRP and WBC) in the obesity. The above information supports the hypothesis that sub-clinical inflammation is a part of metabolic syndrome [4].

CONCLUSION

It can be said that aerobic training decreases inflammatory markers and probably future cardiovascular disease risk in obese men.

REFERENCES

1. Albert, C.M., J. Ma, N. Rifai, M.J. Stampfer and P.M. Ridker, 2002. Prospective study of C-reactive protein, homocysteine and plasma lipid levels as predictors of sudden cardiac death. *Circulation*, 105: 2505.
2. Madjid, M., I. Awan, J.T. Willerson and S.W. Casscells, 2004. Leukocyte count and coronary heart disease. *J. Am. Coll Cardiol.*, 44: 1945-1956.

3. Ridker, P.M., C.H. Hennekens, J.E. Buring and N. Rifai, 2000. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. *N. Engl. J. Med.*, 342: 836-843.
4. Festa, A., R. Dagostino, G. Howard, L. Mykkanen, R.P. Tracy and S.M. Haffner, 2000. Chronic atherosclerosis study. *Circulation*, 102: 42-47.
5. Visser, M., L.M. Bouter, G.M. McQuillan, M.H. Wener and T.B. Harris, 1999. Elevated C-reactive protein levels in overweight and obese adults. *JAMA.*, 282: 2131-2135.
6. Weijenberg, M.P., E.J. Feskens and D. Kromhout, 1996. White blood cell count and the risk of coronary heart disease and all-cause mortality in elderly men. *Arterioscler Thromb Vasc Biol.*, 16: 499-503.
7. Elkind, M.S., J. Cheng, B. Boden-Albala, M.C. Paik and R.L. Sacco, 2001. Elevated white blood cell count and carotid plaque thickness: The northern Manhattan stroke study. *Stroke*, 32: 842-849.
8. Ernst, E., D.E. Hammerschmidt, U. Bagge, A. Matrai and J.A. Dormandy, 1987. Leukocytes and the risk of ischemic diseases. *JAMA.*, 257: 2318-2324.
9. Murohara, T., M. Buerke and A.M. Lefer, 1994. Polymorphonuclear leukocyte-induced vasoconstriction and endothelial dysfunction: Role of selectins. *Arterioscler Thromb*, 14: 1509-1519.
10. Vozarova, B., C. Weyer, R.S. Lindsay, R.E. Pratley, C. Bogardus and P.A. Tataranii, 2002. High development cell count is associated with a worsening of insulin sensitivity and predicts the development of type 2 diabetes. *Diabetes*, 51: 455-461.
11. Pratley, R.E., C. Wilson and C. Bogardus, 1995. Relation of the white blood cell count to obesity and insulin resistance: effect of race and gender. *Obesity Res.*, pp: 563-571.
12. Sesso, H.D., R.S. Paffenbarger and I.M. Lee, 2000. Physical activity and coronary heart disease in men: The Harvard alumni health study. *Circulation*, 102: 975-980.
13. Abramson, J.L. and V. Vaccarino, 2002. Relationship between physical activity and inflammation among apparently healthy middle-aged and older us adults. *Arch. Intern. Med.*, 16: 1286-1292.
14. Wannamethee, S.G., G.D. Lowe, P.H. Whincup, A. Rumley, M. Walker and L. Lennon, 2002. Physical activity and hemostatic and inflammatory variables in elderly men. *Circulation*, 105: 1785-1790.
15. Mattusch, F., B. Dufaux, O. Heine, I. Mertens and R. Rost, 2000. Reduction of the plasma concentration of c-reactive protein following nine months of endurance training. *Int. J. Sports Med.*, 21: 21-24.
16. Smith, J.K., R. Dykes, J.E. Douglas, G. Krishnaswamy and S. Bork, 1999. Long term exercise and atherogenic activity of blood mononuclear cells in persons at risk of developing ischemic heart disease. *JAMA.*, 281: 1722-1727.
17. Williams, M.H., 2002. Nutrition for health, fitness and sport. MC crow Hill. Sixth Edin., pp: 466-467.
18. Wolfe, L., R. Martin, D. Watson, R.D. Lasley and O.E. Bruns, 1985. Chronic exercise and left ventricular structure and function in healthy human subjects. *J. Appl. Physiol.*, 58: 409-415.
19. Morris, C. and V. Froelicher, 1993. Cardiovascular benefits of improved exercise capacity. *Sports Med.*, 16: 225-236.
20. Kramsch, D.M., A.J. Aspen, B.M. Abramowitz, T. Kreimendahl and W.B. Hood, 1981. Reduction of coronary atherosclerosis by moderate conditioning exercise in monkeys on an atherogenic diet. *N. Engl. J. Med.*, 305: 1483-1489.
21. Stratton, J., W. Chandler, R. Schwartz, M.D. Cerqueira, W.C. Levy, S.E. Kahn, V.G. Larson, K.C. Cain, G.C. Beard and I.B. Abrass, 1991. Effects of physical conditioning on fibrinolytic variables and fibrinogen in young and old healthy adults. *Circulation*, 83: 1692-1697.
22. Berliner, J.A., M. Navan, A.M. Fogelman, J.O. Frank I.L. Demer, P.A. Edwards, A.D. Watson and A.J. Lusis, 1995. Atherosclerosis: Basic mechanisms. Oxidation, inflammation and genetics. *Circulation*, 91: 2488-2496.
23. Smith, J. and T. Mc Donald, 1992. Production of serum amyloid A and c-reactive protein by HepG₂ cells stimulated with combinations of cytokines of monocyte conditioned media: the effects of prednisolone. *Clin. Exp. Immunol.*, 90: 293-299.
24. Vasankari, T.J., U.M. Kujala, T.M. Vasankari and M. Ahotupa, 1998. Reduced oxidized LDL levels after a 10-month exercise program. *Med. Sci. Sports Exerc.*, 30: 1496-1501.
25. Straczkowski, M., I. Kowalska, A. Nikolajuk, S. Dzienis-straczkowska, M. Szelachowska and I. Kinalska, 2003. Plasma interleukin 8 concentrations in obese subjects with impaired glucose tolerance. *Cardiovasc Diabetol.*, 2: 5.

26. Nicklas, B.J., T. you and M. Pahor, 2005. Behavioural treatments for chronic systemic inflammation: Effects of dietary weight loss and exercise training. *CMAJ.*, 26: 172-179.
27. Temelkova-kurktschiev, T., G. Siegert, S. Bergmann, E. Henkel, C. Koehler, W. Jaross and M. Hanefeld, 2002. Subclinical inflammation is strongly related to insulin resistance but not to impaired insulin secretion in a high risk population for diabetes. *Metabolism.*, 51: 743-749.
28. Juhan-Vague, I., S. Thompson and J. Jespersen, 1993. Involvement of the hemostatic system in the insulin resistance syndrome: A study of 1500 patients with angina pectoris. The ECAT angina pectoris study group. *Arterioscler Thromb*, 13: 1865-1873.
29. Mayer-Davis, E., D. Agostino, A. Karter, S.M. Haffner, M.J. Rewers and M. Saad, 1998. Bergman RN. Intensity and amount of physical activity in relation to insulin sensitivity: The insulin resistance atherosclerosis study. *JAMA*, 3: 2379-2388.
30. Urakawa, H., A. Katsuki, Y. Sumida, E.C. Gabazza, S. Murashima, K. Morioka, N. Maruyama, N. Kitagawa, T. Tanaka, Y. Hori, K. Nakatani, Y. Yano and Y. Adachi, 2003. Oxidative stress is associated with adiposity and insulin resistance in men. *Jclin Endocrinol Metab.*, 88: 4673-4676.
31. Powers, S.K., L.L. Ji and C. Leeuwenburgh, 1999. Exercise training induced alternations in skeletal muscle antioxidant capacity: a brief review. *Med. Sci. Sports Exerc.*, 31: 987-997.
32. Mohamed-Ali, V., J.H. Pinkney and S.W. Coppack, 1998. Adipose tissue as an endocrine and paracrine organ. *Int. J. Obes.*, 22: 1145-1158.
33. Church, T.S., C.E. Barlow, C.P. Earnest, J.B. Kampert, E.L. Priest and S.N. Blair, 2002. Associations between cardiorespiratory fitness and C-reactive protein in men. *Arterioscler Thromb Vasc. Biol.*, 22: 1869-1876.
34. Van Oostrom, A.J., T.P. Sijmonsma, C. Verseyden, E.H. Jansen, E.J. Dekoning, T.J. Rabelink and M. Castro Cabezas, 2003. Postprandial recruitment of neutrophils may contribute to endothelial dysfunction. *J. Lipid Res.*, 44: 576-583.
35. Kahn, B.B. and J.S. Flier, 2000. Obesity and insulin resistance. *J. Clin. Invest.*, 160: 473-481.
36. Fernandez-Real, J.M., M. Vayreda, C. Richard, C. Gutierrez, M. Broch, J. vendrell and W. Ricart, 2001. Circulating interleukin 6 levels, blood pressure and insulin sensitivity in apparently healthy men and women. *J. Clin. Endocrinol. Metab.*, 86: 1154-1159.
37. Campos, S.P. and H. Baumann, 1992. Insulin is a prominent modulator of the cytokine-stimulated expression of acute-phase plasma protein genes. *Mol. Cell. Biol.*, 12: 1789-1797.